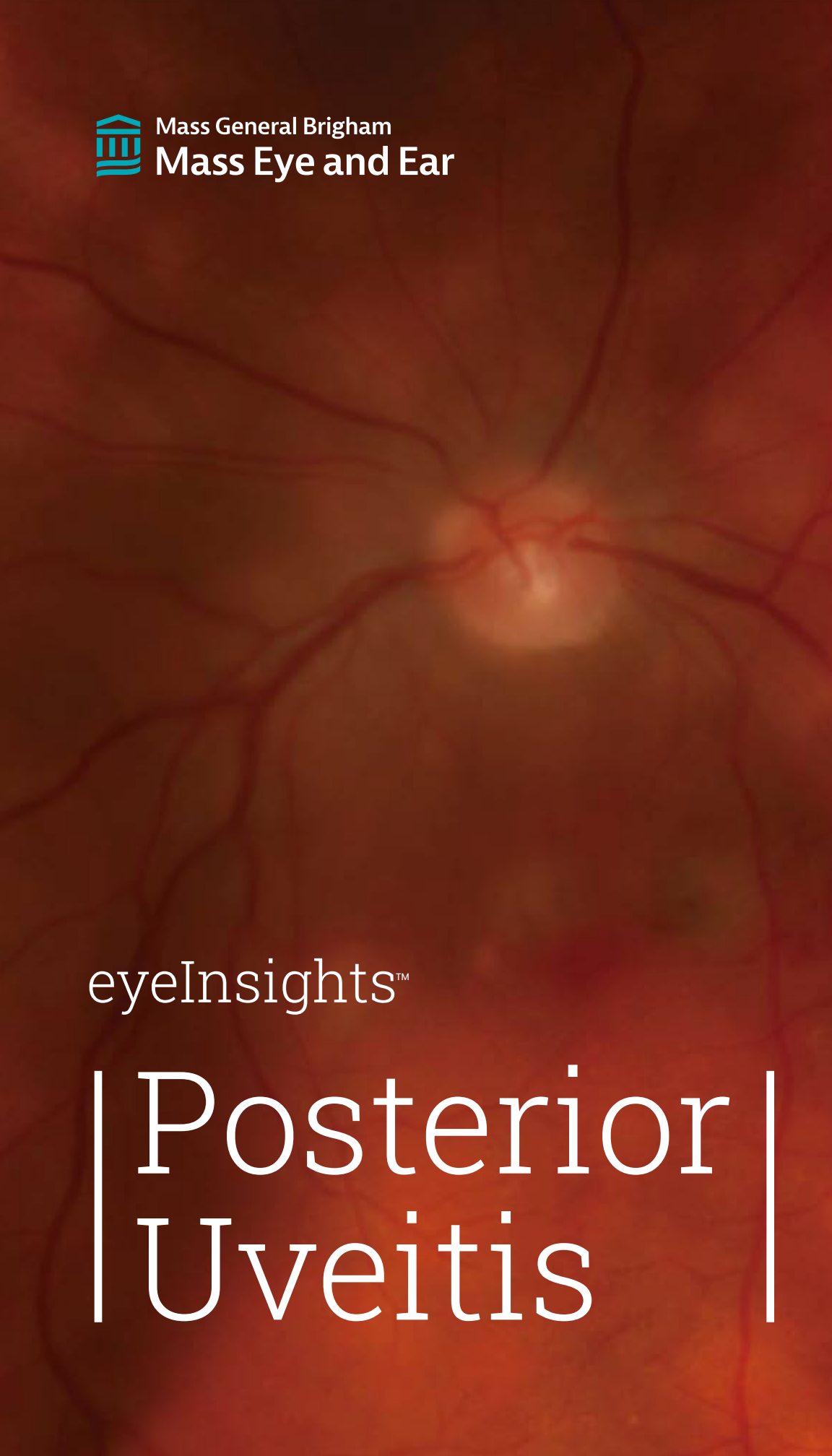

Mass General Brigham
Mass Eye and Ear
eyeInsights™
Posterior Uveitis

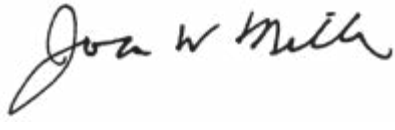
Dear Colleagues,

In this issue of *eye Insights*, we take a close look at posterior uveitis. Inside, you'll find techniques and tips for evaluating and managing patients with this condition.

Due to its many etiologies, posterior uveitis can be challenging to treat until the cause of the inflammation is identified. Therefore, we have included some helpful guidelines and risk factors to aid in distinguishing the root cause.

Once posterior uveitis is suspected, referral to a specialist is recommended. For a list of doctors who specialize in treating posterior uveitis, please visit the online American Academy of Ophthalmology directory.

We hope you find this issue of *eye Insights* useful in your practice. Back issues are available online at masseyeandear.org. If you have questions or comments, please email us at eyeinsights@meei.harvard.edu.




**Joan W. Miller, MD**

*David Glendenning Cogan Professor of Ophthalmology and Chair, Department of Ophthalmology, Harvard Medical School*

*Chief of Ophthalmology, Massachusetts Eye and Ear and Massachusetts General Hospital*

*Ophthalmologist-in-Chief, Brigham and Women's Hospital*

# What is posterior uveitis?

Posterior uveitis, or choroiditis, refers to inflammation of the choroid. It can affect the retina and/or optic nerve and lead to permanent loss of vision.

## What causes posterior uveitis?

Posterior uveitis can be infectious or non-infectious.

*Many non-infectious cases are idiopathic.*

### Common non-infectious causes

- Sarcoidosis
- Birdshot chorioretinopathy
- Behcet's disease
- Presumed ocular histoplasmosis
- Certain medications
- Vogt-Koyanagi-Harada syndrome

### Common infectious causes

- Toxoplasmosis
- Syphilis
- Tuberculosis
- Herpes family of viruses

## Prevalence

Non-infectious posterior uveitis is uncommon, affecting about 10 people per 100,000 persons in the United States. It occurs most often in adults between 20 and 50 years of age. Infectious posterior uveitis is more common in developing countries.

## Risk factors

Risk factors for non-infectious posterior uveitis include having an underlying autoimmune or immune-mediated disease, such as sarcoidosis. Risk factors for infectious posterior uveitis vary depending on the etiology. For example, eating undercooked meat and being from an endemic region, such as Central or South America, are risk factors for toxoplasmosis, which can lead to uveitis.

# Ask the expert

**Lucia Sobrin, MD, MPH**

*Charles Edward Whitten Professor of Ophthalmology, Harvard Medical School*

*Associate Chief of Clinical Data Science*
*Director, Morse Laser Center*
*Mass Eye and Ear*

## Diagnosis

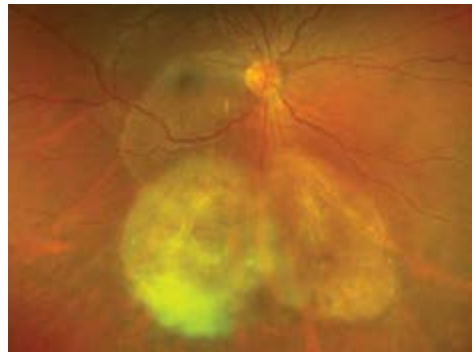
The most common symptoms of posterior uveitis are blurred vision and floaters, and the most common signs are chorioretinal infiltrates and vitreous cells.

Posterior uveitis is diagnosed by slit lamp examination and indirect ophthalmoscopy. Imaging modalities, including fundus autofluorescence, fluorescein angiography, indocyanine green angiography, and optical coherence tomography, are key to establishing the extent of disease, identifying complications such as macular edema, and for monitoring disease progression or remission.

A work up for underlying etiologies is always part of the diagnostic process and is particularly important to distinguish between infectious and non-infectious etiologies. The work up should be guided by the history, review of systems, and examination and imaging findings. For example, HLA A29 testing for birdshot chorioretinopathy should only be done if the examination or imaging show fundus lesions that are consistent with the disease, as approximately 10% of patients of European descent will be HLA-A29 positive, but only a very small minority of these patients will ever develop birdshot chorioretinopathy. However, there are some etiologies that should always be tested for. In particular, serologies for syphilis and a chest X-ray to evaluate for sarcoidosis and tuberculosis should be ordered. Intraocular lymphoma can masquerade as posterior uveitis and should be considered particularly in older patients and those who do not respond to treatment for uveitis as expected.

# Treatment of infectious uveitis

Treatment of infectious uveitis is dependent on the specific microbe.



**RIGHT** Placoid syphilitic retinitis: yellow, deep retinal infiltrates in a patient with positive serologies for syphilis.

# Treatment of non-infectious uveitis

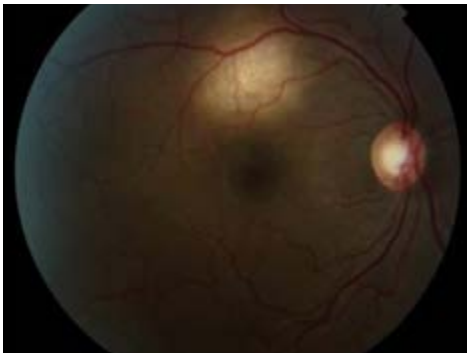
## Anti-inflammatories

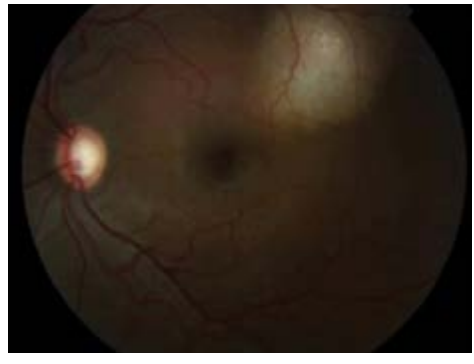
Periocular, intravitreal, or systemic steroids are the mainstay of the acute treatment of non-infectious posterior uveitis. Topical steroids do not penetrate sufficiently to the posterior segment to control inflammation in posterior uveitis.

In addition to direct injection of corticosteroid formulations like triamcinolone into the periocular or intravitreal space, there are three intravitreal corticosteroid delivery devices currently approved for treatment of non-infectious posterior uveitis: the injectable dexamethasone 0.7 mg implant (Ozurdex), the injectable fluocinolone 0.18 mg implant (Yutiq) and the surgically implanted fluocinolone 0.59 mg implant (Retisert).

## Side effects

Potential side effects of corticosteroids include increased intraocular pressure and cataracts (local delivery) and weight gain, diabetes and osteopenia (systemic delivery), which make them less desirable for long-term treatment of chronic forms of uveitis.





**ABOVE** Sarcoidosis-related bilateral choroidal granulomas in a patient with lymph node biopsy demonstrating non-caseating granulomas.

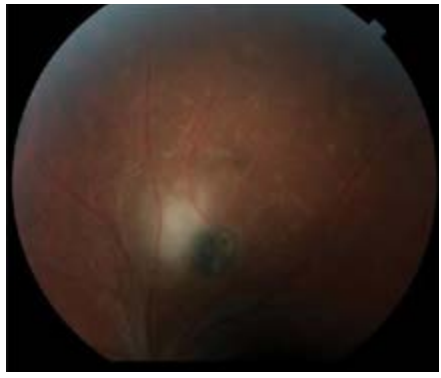
# Treatment of chronic, non-infectious uveitis

## Systemic therapy

For chronic disease, steroid-sparing systemic therapies are necessary. While the two fluocinolone implants can provide control for up to three years, there is evidence from the Multicenter Uveitis Steroid Treatment (MUST) Trial that outcomes with the surgically implanted fluocinolone implant may be slightly worse than with systemic immunomodulatory therapy at seven years (Kempen et al. *JAMA* 2017).

Conventional immunomodulatory medications, such as methotrexate and mycophenolate, are the most commonly used agents, but biologic agents are being increasingly used. Adalimumab, a self-injectable biologic that blocks tumor necrosis factor alpha (TNF-alpha), is approved for the treatment of non-infectious posterior uveitis. Because these agents are associated with potential side effects, including susceptibility to infections and hepatic toxicity, these agents require co-management with a uveitis specialist or rheumatologist trained in the use of these medications.

At Mass Eye and Ear, our uveitis specialists manage these medications and direct an infusion center dedicated to ocular inflammation to deliver intravenous biologics for the most severe uveitis patients.



**ABOVE** Toxoplasmosis chorioretinitis reactivation: there is a yellow/white infiltrate adjacent to a pigmented scar.

## Safety of immunomodulatory agents

Immunomodulatory agents are safe and associated with excellent outcomes. The Systemic Immunosuppressive Therapy for Eye Diseases (SITE) study, led by Dr. John Kempen, Director of Epidemiology at Mass Eye and Ear, found that patients treated with conventional immunomodulatory therapies have no increased risk of overall mortality or cancer-related mortality (Kempen et al. *BMJ* 2009). The MUST trial has shown that patients treated with systemic immunomodulatory therapies are able to maintain visual acuity improvement over seven years (Kempen et al. *JAMA* 2017).

## Future therapies

Still, not all patients respond to or tolerate available agents, and there is a need for additional therapies. Multiple medications are currently in clinical trials for the treatment of non-infectious uveitis. Researchers are exploring new mechanisms, including intravenous interleukin 6 (IL-6) inhibitor therapy (sarilumab), oral Janus kinase (JAK) inhibitors (filgotinib), and intravitreal sirolimus (an mTOR inhibitor).

Checkpoint inhibitors are becoming more widely used in the management of cancer, so it is important for the ophthalmologist to examine the medication list carefully in a patient with new-onset uveitis.

## Uveitis associated with immune checkpoint inhibitors

- Immune checkpoint inhibitors are used increasingly to treat a variety of cancers, including metastatic melanoma and non-small cell lung cancer.
- These drugs work by activating T-cells for attack against cancer cells.
- They are associated with a variety of immune-related adverse events that most commonly affect the skin, GI tract, lungs, and endocrine glands. Ocular side effects are seen in ~1% of cases, with uveitis and dry eyes being the most common. Orbital inflammation can also occur.
- In cases of uveitis, the most common presentation is bilateral anterior uveitis, but posterior uveitis, panuveitis, retinal vasculitis, and a Vogt-Koyanagi-Harada-like syndrome can also be seen.
- Clear and timely communication with the oncologist is paramount.
- Treatment of checkpoint inhibitor-induced uveitis is primarily with local steroids (topical, periocular, intravitreal depending on the site of inflammation). Systemic steroids could diminish checkpoint inhibitor activity.
  - *In milder cases, checkpoint inhibitor treatment can be continued.*
  - *In severe cases consult with oncologist, treatment may need to be discontinued.*

## Immune checkpoint inhibitors associated with uveitis

- Ipilimumab
- Nivolumab
- Pembrolizumab
- Cemiplimab
- Avelumab
- Durvalumab
- Atezolizumab

eyeInsights™ November 2021

**Editor-in-Chief:**
Joan W. Miller, MD

**Managing Editor:**
Matthew F. Gardiner, MD

**Publications Manager:**
Jessica O'Donnell

**Clinical Advisory Group:**
Deeba Husain, MD
Alice Lorch, MD, MPH
Ankoor S. Shah, MD, PhD

**Contributor:**
Lucia Sobrin, MD, MPH

**Design:**
Stone Design Studio

**Photography:**
Licensed from istock.com
Clinical Images from
Lucia Sobrin, MD, MPH

Published biannually, *eye Insights* offers the ophthalmology community best practice information from Massachusetts Eye and Ear specialists.

We welcome your feedback. Send comments to:
**eyeinsights@meei.harvard.edu**

Mass General Brigham
Mass Eye and Ear

Mass General Brigham
Mass Eye and Ear

243 Charles Street
Boston, MA 02114

masseyeandear.org



eyeInsights™